

REMARKS/ARGUMENTS

Claims 46, 49-53, 81, 186, 194-199, 217-220, 246, 272-273 and 280-299 are pending. Claims 46, 81, and 186 have been amended herein. The Examiner has indicated that Claims 272 and 273 are allowed and has indicated that claims 53, 199, 281, 287, 288 and 294 are objected to as being dependent upon rejected claims 46 and 186, but would be allowable if rewritten in independent form. Applicants are unclear as to the status of claims 286 and 293 as they are not included in the rejections given by the Examiner and were also not included in the claims that were objected to as being dependent upon rejected claims. Applicants request clarification of the status of claims 286 and 293.

Claim Rejections Under 35 U.S.C. § 103-Reynolds in view of Jiang and Jacobson:

The Examiner has rejected Claims 46, 49-52, 81, 186, 194-198, 217, 219, 220, 246, 280, 282-285, 289-292, 295 and 297-299 under 35 U.S.C. § 103(a) as being obvious over Reynolds E.C. (U.S. Patent No. 6,780,844) (herein referred to "Reynolds") in view of Jiang et al., *J. Agric. Food Chem.*, **48**:990-994 (2000) (herein referred to as "Jiang") and Jacobson et al., (U.S. 2002/0128298) (herein referred to as "Jacobson"). The Office action asserts that Reynolds teaches a **complex** containing phosphopeptide stabilized amorphous calcium fluoride phosphate and teaches a pharmaceutical composition comprising said complex, wherein the composition is a dental composition in a form of a gel, solid, powder or cream for treating dental caries or tooth decay wherein the dental cream is toothpaste; that the phosphopeptide is a **casein** protein fragment; that the phosphopeptide stabilizes the amorphous calcium phosphate (ACP); and that the stabilized ACP is most soluble wherein the stabilized and soluble ACP prevents caries and increases calcium bioavailability. The Office action does states that Reynolds **does not** expressly teach that the phospholipid is **phosvitin or a fragment thereof** nor teaches that the phosphopeptide is **partially phosphorylated**, e.g., 65% de-phosphorylated. The Office action asserts that Jiang teaches that the partially phosphorylated (with 35% phosphates retention) phosvitin phosphopeptide (PPP) inhibits calcium phosphate precipitation wherein 35% phosphate retention which is considered to be equivalent to about 65% dephosphorylation thereof shows the highest capability of solubilization of the insoluble calcium phosphates. The Office action only applies the teachings of Jacobson to claims 217 and 295 and asserts that

Jacobson teaches that administration of dental composition toothpaste is a topical administration route.

The Office action concludes that it would have been obvious to one of ordinary skill in the art at the time the invention was made to prepare the pharmaceutical composition such as in a gel or powder form of dental composition which comprises the de-phosphorylated (~65%) phosvitin or fragment thereof and that one would have substituted the phosvitin phosphopeptide for casein phosphopeptide (CPP) and would have used the phosvitin phosphopeptide (PPP) to form said **complex** in said pharmaceutical composition.

Applicant respectfully traverses this rejection. First, the Applicant reiterates that the Applicant did make an election without traverse in response to the previous restriction requirement because the Applicant agreed with the Examiner that the pharmaceutical compositions of the presently pending claims are patentably distinct (*i.e.*, novel and not obvious) from oral care compositions, such as the dental compositions disclosed by Reynolds (see below). The Applicant maintains that the Examiner's reliance on teachings in Reynolds and other references concerning dental compositions and oral care is still considered improper.

However, in order to expedite prosecution of the application, Claims 46 and 186 have been amended so that they cover a pharmaceutical composition consisting essentially of a phosvitin or fragment thereof. Reynolds teaches complexes of amorphous calcium phosphate (ACP) with certain phosphopeptides. See, *e.g.*, column 2, lines 51-55 of Reynolds. As concluded by the Examiner: "One of ordinary skill in the art would have substitute the phosvitin phosphopeptides [of Jiang] for the casein phosphopeptide [of Reynolds] to form said complex in said pharmaceutical composition." See page 5 of the Office action. The present claims claim phosvitin (the protein) or fragments of the phosvitin protein as such (*i.e.* not complexed) in a pharmaceutical composition, and the above amendments of Claims 46 and 186 are intended to make this status clear. In particular, the phosvitin or fragments thereof of the present claims are in a form that can be phosphorylated to reduce unwanted increased phosphorylation and to cause the therapeutic effects taught by the present application. See, *e.g.*, page 2, lines 22-31, of the present application.

In addition, claim 81 has been amended to specify at least 70% dephosphorylation. Support for this amendment is found in, *e.g.*, Example 2 of the present application.

In regards to the teachings of Jacobson that “administration of dental composition toothpaste is a topical administration route” (Office action pg. 3), Applicants contend that there would be no motivation for one of skill in the art to combine the teachings of Jacobson with the teachings of Reynolds and/or Jiang in regards to Claims 217 and 295, as there is no teaching in Jacobson of any pharmaceutical compositions with the phosphopeptides disclosed by Reynolds and Jiang. Jacobson discloses the mode by which nicotinic acid or ester is administered ([0040] of Jacobson).

The Examiner bears the burden of establishing a *prima facie* case of obviousness (Section 103). In determining obviousness, one must focus on Applicant’s invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 U.S.P.Q.2d 1241, 1246 (Fed Cir. 1991). Applicant points out that it is axiomatic that a claimed invention is not obvious solely because it is composed of elements that are all individually found in the prior art. See, e.g., *In re Rouffet*, 149 F.3d 1350, 1357, 47 U.S.P.Q.2D (BNA) 1453, 1457 (Fed. Cir. 1998), and that it is impermissible to use the claimed invention as an instruction manual or ‘template’ to piece together the teaching of the prior art so that the claimed invention is rendered obvious.” *In re Fritch*, 972 F.2d 1260, 1266, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992). It appears that the rejection uses this “template” approach, in which the invention has been decomposed into its constituent elements, the elements were noted in the prior art, and then concluded that it is easy to reassemble these elements into the invention. This is particularly shown by the Examiner’s use of Jacobson. Such an approach “is a forbidden ex post analysis.” *In re Mahurkar Patent Litigation*, 831 F. Supp. 1354, 28 USPQ2d, 1801 (N.D. Ill. 1993), *aff’d*, 71 F.3d 1573, 37 USPQ2d 1138 (Fed. Cir. 1995).

Applicants submit that there is no suggestion or motivation in the references to make the combination and respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Claim Rejections Under 35 U.S.C. § 103-Reynolds in view of Jiang, Jacobson and Shuch:

The Examiner has rejected Claims 186, 194, 218 and 296, under 35 U.S.C. § 103(a) as being obvious over Reynolds E.C. (U.S. Patent No. 6,780,844) (herein referred to “Reynolds”) in view of Jiang et al., *J. Agric. Food Chem.*, **48**:990-994 (2000) (herein referred to as Jiang) and Jacobson et al., (U.S. 2002/0128298) (herein referred to as “Jacobson”) and further in view of Shuch et al., (U.S. Patent No. 6, 503,483) (herein referred to as “Shuch”). The Office action uses the teachings of Reynolds, Jiang and Jacobson as above and further states that these three

references do not expressly teach that the formulated composition is in drop form. The Office action asserts that Shuch teaches that oral delivery system, i.e., formulation can be candy-gum "drops".

Applicants contend that the type of drops claimed in the present claims are not, and would not have been obvious in view of, candy-gum drops as taught by Shuch, and the Examiner's use of Shuch is another example of the Examiner's use of the "template" approach. Moreover, the teachings of Shuch do not make up for the deficiencies of Reynolds, Jiang and Jacobson as discussed above. Therefore, there is no suggestion or motivation in the references to make the combination, and Applicants respectfully request that the rejection under 35 U.S.C. § 103(a) be withdrawn.

Based upon the foregoing, Applicants believe that all pending claims are in condition for allowance and such disposition is respectfully requested. In the event that a telephone conversation would further prosecution and/or expedite allowance, the Examiner is invited to contact the undersigned.

Respectfully submitted,
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